

Figure 1A

See ID No.:

6	mouse_E3 $\alpha$ II	MASEMEPEVQ AI D-RSLLEC SAEII AGRWL QATDL NREVV QHLAHCVPKI	49
4	human_E3 $\alpha$ II	MASELEPEVQ AI D-RSLLEC SAEII AGKWL QATDL TREVY QHLAHYVPKI	49
15	mouse_E3 $\alpha$ II	MADEEMDGAE RMDVSPPEPPL APQRPAWSMD QQVDFYTAFL HHLAQQLVPEI	50
2	human_E3 $\alpha$ II	MADEEAGGTE RMEI SAELPQ TPQRLASWMD QQVDFYTAFL HHLAQQLVPEI	50
Consensus			
MA. E. . . . .	D. . . . .	A. . . . .	W. Q. . D. . . . .
6	mouse_E3 $\alpha$ II	YCRGPNPFPQ KEDTLAQHIL LGPMEWYI CA EDPALGFPKL EQANKPSHLC	99
4	human_E3 $\alpha$ II	YCRGPNPFPQ KEDMLAQHVL LGPMEWYLCG EDPAFGFPKL EQANKPSHLC	99
15	mouse_E3 $\alpha$ II	YFAEMDPDLE KQEESVQMSI LTPLEWYLFQ EDPDI CLEKL KHSG-AFQLC	99
2	human_E3 $\alpha$ II	YFAEMDPDLE KQEESVQMSI FTPLEWYLFQ EDPDI CLEKL KHSG-AFQLC	99
Consensus			
Y. . . . .	P. . . . .	K. . . . .	Q. . . . .
6	mouse_E3 $\alpha$ II	GRVFKVGEPT YSCRDCAVDP TCVLCMCCFL GSI HRDHRYR MTTSGGGFC	149
4	human_E3 $\alpha$ II	GRVFKVGEPT YSCRDCAVDP TCVLCMCCFL GSI HRDHRYR MTTSGGGFC	149
15	mouse_E3 $\alpha$ II	GKVFKSGETT YSCRDCAI DP TCVLCMDCFQ SSVHKNHRYK MHTSTGGGFC	149
2	human_E3 $\alpha$ II	GRVFKSGETT YSCRDCAI DP TCVLCMDCFQ DSVHKNHRYK MHTSTGGGFC	149
Consensus			
GRVFK. GE. T	YSCRDCAI. DP	TCVLCM. CF.	. S. H. . HRY. M. TS. GGGFC
6	mouse_E3 $\alpha$ II	SSEVVEEEDP LVHLSEDVI A RTYNI FAI MF	199
4	human_E3 $\alpha$ II	DCGDTEAWKE GPYCQKHKLS TSEIEEEEEDP LVHLSEDVI A RTYNI FAI TF	199
15	mouse_E3 $\alpha$ II	DCGDTEAWKE GPYCQKHEL N TSEIEEEEEDP RAGTTKESLH -CPLNEEVIA QARRIFPSVI	198
2	human_E3 $\alpha$ II	DCGDTEAWKT GPFCVNHEPG RAGTI KENS R -CPLNEEVIV QARKIFPSVI	198
Consensus			
DCGDTEAWK. GP. C. HE. . . . .	DCGDTEAWK. GP. C. HE. . . . .	DCGDTEAWK. GP. C. HE. . . . .	E. . . . .

## Figure 1B

6	mouse_E3 $\alpha$ II	RYAVDI LTWE KESEL PEDLE VAEKSDTYYC MLFNDEVHTY EQVI YTLLQKA	249
4	human_E3 $\alpha$ II	RYAVEI LTWE KESEL PADLE MWEKSDTYYC MLFNDEVHTY EQVI YTLLQKA	249
15	mouse_E3 $\alpha$ I	KYIVEMTI WE EEKELPPELQ I REKNERYYC VLFNDEHHSY DHVI YSLQRA	248
2	human_E3 $\alpha$ I	KYVVEMTI WE EEKELPPELQ I REKNERYYC VLFNDEHHSY DHVI YSLQRA	248
	Consensus	.Y. VE...WE .E. ELP..L. .EK...YYC .LFNDE. H. Y ..VI Y. LQ. A	250
6	mouse_E3 $\alpha$ II	VNCCTQKEAI G FATTVDRDGR RPVRYGDFQY CDQAKTVI VR NTSRQTK- PL	298
4	human_E3 $\alpha$ II	VNCCTQKEAI G FATTVDRDGR RSVRYGDFQY CEQAKSVI VR NTSRQTK- PL	298
15	mouse_E3 $\alpha$ I	LDCELAEAQL HTTAI DKEGR RAVKAGVYAT CQEAKEDI KS HSENVSQHPL	298
2	human_E3 $\alpha$ I	LDCELAEAQL HTTAI DKEGR RAVKAGAYAA CQEAKEDI KS HSENVSQHPL	298
	Consensus	..C...EA... .T..D..GR R. V..G.... C..AK..I.....PL	300
6	mouse_E3 $\alpha$ II	KVQVMHSSVA AHQNFGLKAL SWLGSVI GYS DGLRRILCQV GLQE GDPGEN	348
4	human_E3 $\alpha$ II	KVQVMHSSIV AHQNFGLKLL SWLGSII GYS DGLRRILCQV GLQE GDPGEN	348
15	mouse_E3 $\alpha$ I	HVEVLHSVVM AHQKFAIRLG SWMNKIMYS SDFRQIFCQA CLVEEPGSEN	348
2	human_E3 $\alpha$ I	HVEVLHSIIM AHQKFAIRLG SWMNKIMYS SDFRQIFCQA CLREEPDSEN	348
	Consensus	.V. V. HS... AHQ. F. L. L. SW...I...YS ...R. I. CQ. L. E. PD. EN	350

## Figure 1C

6	mouse_E3 $\alpha$ II	SSLVDR <sub>L</sub> M <sub>N</sub> DSKLWKGARS	VYHQLFMS <sub>L</sub> LMDLKYYKKLF	ALRFAKNYRQ	398
4	human_E3 $\alpha$ II	SSLVDR <sub>L</sub> M <sub>S</sub> DSKLWKGARS	VYHQLFMS <sub>L</sub> LMDLKYYKKLF	AVRFAKNYQQ	398
15	mouse_E3 $\alpha$ I	PCL <sub>I</sub> SRLM <sub>L</sub> W DAKLYKGARK	I LHELI FSSF FME <sup>M</sup> EYKKLF	AM <sup>E</sup> FVKKYYKQ	398
2	human_E3 $\alpha$ I	PCL <sub>I</sub> SRLM <sub>L</sub> W DAKLYKGARK	I LHELI FSSF FME <sup>M</sup> EYKKLF	AMEFVKKYYKQ	398
	Consensus	... L... RLM... D. KL. KGAR. ... H. L... SS...	... M... YKKLF A... F. K. Y. Q	400	
6	mouse_E3 $\alpha$ II	LQRDFMEDDH ERAVSVTALS	VQFFTAPTLA RMLTEENLM TVI I KAFMDH	448	
4	human_E3 $\alpha$ II	LQRDFMEDDH ERAVSVTALS	VQFFTAPTLA RMLTEENLM SII I KTFMDH	448	
15	mouse_E3 $\alpha$ I	LQKEYI SDDH ERSI SI TALS	VQMLTVPTLA RHLI EEQNVI SVI TETLLEV	448	
2	human_E3 $\alpha$ I	LQKEYI SDDH DRSI SI TALS	VQMF <sup>M</sup> TVPTLA RHLI EEQNVI SVI TETLLEV	448	
	Consensus	... LQ... . . . DDH ER... S. TALS	VQ. FT. PTLA R. LI . E. N. . SVI . . T...	450	

## Figure 1D

SEQ ID NO:	mouse_E3 $\alpha$ II	human_E3 $\alpha$ II	mouse_E3 $\alpha$ II	human_E3 $\alpha$ II	mouse_E3 $\alpha$ I	human_E3 $\alpha$ I	mouse_E3 $\alpha$ I	human_E3 $\alpha$ I	Consensus	mouse_E3 $\alpha$ II	human_E3 $\alpha$ II	mouse_E3 $\alpha$ II	human_E3 $\alpha$ II	mouse_E3 $\alpha$ I	human_E3 $\alpha$ I	mouse_E3 $\alpha$ I	human_E3 $\alpha$ I	Consensus	mouse_E3 $\alpha$ II	human_E3 $\alpha$ II	mouse_E3 $\alpha$ II	human_E3 $\alpha$ II	mouse_E3 $\alpha$ I	human_E3 $\alpha$ I	mouse_E3 $\alpha$ I	human_E3 $\alpha$ I	Consensus	
6	LKH RDAQGRF	LKH RDAQGRF	QFERYTALQA	FKFRRVQSLI	L DL KYVLI SK	PTEW <del>S</del> DEL RQ	498			KFL QGFD AFL	ELL KCMQGMD	P I T RQV GQH I	EMEPWEAAF	TL QM <del>K</del> L THV I	548				S M V QDW CAL D	E KV L I E A Y K K	C L A V L T Q C H G	GFT DGE QP I T	L S I C G H S V E T	598				
4	LRH RDAQGRF	LRH RDAQGRF	QFERYTALQA	FKFRRVQSLI	L DL KYVLI SK	PTEW <del>S</del> DEL RQ	498			KF L E G F D AFL	ELL KCMQGMD	P I T RQV GQH I	EMEPWEAAF	TL QM <del>K</del> L THV I	548				S M V QDW C A S D	E KV L I E A Y K K	C L A V L M Q C H G	G Y T D G E Q P I T	L S I C G H S V E T	598				
15	LPE YL DRNN-	LPE YL DRNN-	KFN- F QG Y S Q	D K L G R V Y A V I	CDL KYI L I SK	P V I W T E R L R A	496			Q F L E G F R S F L	K I L T C M Q G M E	E I R R Q V G Q H I	E V D P D M E A A I	A I Q M Q L K N I L	546				L M F Q E W C A C D	E D L L L V A Y K E	C H K A V M R C S T	N F M S T K T V -	V Q L C G H S L E T	595				
2	human_E3 $\alpha$ I	human_E3 $\alpha$ I	LPE YL DRNN-	KFN- F QG Y S Q	D K L G R V Y A V I	CDL KYI L I SK	P T I W T E R L R M	496		L . . . . .	K . . . . .	R V . . . . .	E . . P . W E A A .	Q M L . . . . .	550				L M F Q E W C A C D	E E L L L V A Y K E	C H K A V M R C S T	S F I S S S K T V -	V Q S C G H S L E T	595				
	Consensus	Consensus	L . . . . .	F . . . . .	K . . . . .	R V . . . . .	I . . . . .											M Q . W C A . D	E . . L . A Y K .	C . . . . . M C . . .	F . . . . .	C G H S . E T	600					

## Figure 1E

6	mouse_E3 $\alpha$ II	I RYCVSQEKV SI HLPISRLL AGLHVLLSKS EVAYKFPELL PLSELSPPM <del>L</del>	648
4	human_E3 $\alpha$ II	I YCVSQEKV SI HLPVSRLL AGLHVLLSKS EVAYKFPELL PLSELSPPM <del>L</del>	648
15	mouse_E3 $\alpha$ I	KSYKVS <del>ED</del> LV SI HLP <del>S</del> RTL AGLHVRLSRL GAI SRLHEFV PFD <del>S</del> QVEVL	645
2	human_E3 $\alpha$ I	KSYRV <del>SE</del> DLV SI HLP <del>S</del> RTL AGLHVRLSRL GAVSRLHEFV SFEDFQVEVL	645
	Consensus	.. Y. VS. . . V SI HLP. SR. L AGLHV. LS. . . . . E. . P. . . . . L	650
6	mouse_E3 $\alpha$ II	I EHPLRCLVL CAQVHAGMMR RNGFSSLVNQI YYYHNVKCRR EMFDKDI VML	698
4	human_E3 $\alpha$ II	I EHPLRCLVL CAQVHAGMMR RNGFSSLVNQI YYYHNVKCRR EMFDKDVVML	698
15	mouse_E3 $\alpha$ I	VEYPLRCLVL VAQVVAEMMR RNGLSSLISQV FYYQDVVKCRE EMYDKDI I ML	695
2	human_E3 $\alpha$ I	VEYPLRCLVL VAQVVAEMMR RNGLSSLISQV FYYQDVVKCRE EMYDKDI I ML	695
	Consensus	. E. PLRCLVL . AQV. A. MMR RNG. SL. . Q. . YY.. VKCR. EM. DKDI . ML	700
6	mouse_E3 $\alpha$ II	QTGVSMWDPN HFLM <del>M</del> MLSRF ELYQLFSTPD YGKRFSSSEVT HKD <del>V</del> VQNNNT	748
4	human_E3 $\alpha$ II	QTGVSMWDPN HFLM <del>M</del> MLSRF ELYQI FSTPD YGKRFSSSEIT HKD <del>V</del> VQNNNT	748
15	mouse_E3 $\alpha$ I	QI GAS <del>I</del> MDPN KFLLLVLQRY EL---TDA FNKTI ST--K DQDLI KQYNT	738
2	human_E3 $\alpha$ I	QI GASLMDPN KFLLLVLQRY EL---AEA FNKTI ST--K DQDLI KQYNT	738
	Consensus	Q. G. S. MDPN . FL. . . L. R. EL. . . . T. . . K. . S. . . . D. . . Q. NT	750

## Figure 1F

6	mouse_E3 $\alpha$ II	LI EEM L Y L I I	ML VGER F N P G	V G Q V A A T D E I	K R E I I H Q L S I	K P M A H I S E L V K	798
4	human_E3 $\alpha$ II	LI EEM L Y L I I	ML VGER F S P G	V G Q V N A T D E I	K R E I I H Q L S I	K P M A H I S E L V K	798
15	mouse_E3 $\alpha$ I	LI EEM L Q V L I	Y I V G E R Y V P G	V G N V T R E E V I	M R E I I T H L L C I	E P M P H I S A I A R	788
2	human_E3 $\alpha$ I	LI EEM L Q V L I	Y I V G E R Y V P G	V G N V T K E E V T	M R E I I H L L C I	E P M P H I S A I A K	788
Consensus							
		LI EEM . . . I	Y I V G E R . . . I	V G E R . . . P G	V G . V . . . I	RE I I H . L . I	P M H S . . . K
							800
6	mouse_E3 $\alpha$ II	SL P E D E N K E T	G M E S V I E S V A	H F K K P G L T G R	G M Y E L K P E C A	K E F N L Y F Y H F	848
4	human_E3 $\alpha$ II	SL P E D E N K E T	G M E S V I E A V A	H F K K P G L T G R	G M Y E L K P E C A	K E F N L Y F Y H F	848
15	mouse_E3 $\alpha$ I	N L P E N E N N E T	G L E N V I N K V A	T F K K P G V S G H	G V Y E L K D E S L	K D F N M Y F Y H Y	838
2	human_E3 $\alpha$ I	N L P E N E N N E T	G L E N V I N K V A	T F K K P G V S G H	G V Y E L K D E S L	K D F N M Y F Y H Y	838
Consensus							
		L P E . E N . E T	G . E . V I . . V A	. F K K P G . . G	G . Y E L K . E . .	K . F N . Y F Y H .	850
6	mouse_E3 $\alpha$ II	S R A E Q S K A E E	A Q R K L K R E N K	E D T A L P P P A L	P P F C P L F A S L	V N I L Q C D V M L	898
4	human_E3 $\alpha$ II	S R A E Q S K A E E	A Q R K L K R Q N R	E D T A L P P P V L	P P F C P L F A S L	V N I L Q S D V M L	898
15	mouse_E3 $\alpha$ I	S K T Q H S K A E H	M Q K K R R K Q E N	K D E A L P P P P P	P E F C P A F S K V	V N L L S C D V M	888
2	human_E3 $\alpha$ I	S K T Q H S K A E H	M Q K K R R K Q E N	K D E A L P P P P P	P E F C P A F S K V	I N L L N C D I M M	888
Consensus							
		S . . . S K A E .	. Q . K . . . Q . .	. D . A L P P P .	P . F C P . F . . .	V N . L . C D V M	900

## Figure 1G

SEQ ID NO:	mouse_E3 $\alpha$ II	YI MGTI LQWA VEHHGSAWSE SML QRVL HLI	GMAL QEEKHH LENAVE GHVQ 948
6	human_E3 $\alpha$ II	CI MGTI LQWA VEHNGYAWSE SML QRVL HLI	GMAL QEEKQH LENVTEHVV 948
4	mouse_E3 $\alpha$ I	YI LRTI FERA VDTESNLWTE GML QMAFHI L	ALGLLEEKQQ LQKAPEEEV- 937
15	mouse_E3 $\alpha$ I	YI LRTVFERA IDTDSNLWTE GML QMAFHI L	ALGLLEEKQQ LQKAPEEEV- 937
2	human_E3 $\alpha$ I	YI .. TI .. A V .. . . . . W E . MLQ .. H .	... L. EEKQ. L .. A. EE. V. 950
	Consensus		
6	mouse_E3 $\alpha$ II	TFTFTQKI SK PGDAPHNSPS I LAMLETQN	APSLEAHKDM I RWLLKMFNA 998
4	human_E3 $\alpha$ II	TFTFTQKI SK PGEAPKNSPS I LAMLETQN	APYLEVHKDM I RW LKTFNA 998
15	mouse_E3 $\alpha$ I	AFDFYHKASR LGSSAMNAQN I QMLLERLKKG	I PQLEGQKDM I TW LQMFDT 987
2	human_E3 $\alpha$ I	TFDFYHKASR LGSSAMNI QM L---LEKLKG	I PQLEGQKDM I TW LQMFDT 984
	Consensus	TF. F. . K. S. . G. . . N. . . I . . . LE. L. . . P. LE. . KDM I . WL. MF. .	1000
6	mouse_E3 $\alpha$ II	I KKI RE-- CS SSSPVAEAEG TI MESSRDK	DKAERKRKAE I ARLRREKIM 1046
4	human_E3 $\alpha$ I	VKKMRE-- SS PTSPVAETEG TI MESSRDK	DKAERKRKAE I ARLRREKIM 1046
15	mouse_E3 $\alpha$ I	VKRLREKSCL VVATSGLEC I KSEEITHDK	EKAERKRKAE AARLHRQKIM 1037
2	human_E3 $\alpha$ I	VKRLREKSCL I VATTSGSES I KNDEITHDK	EKAERKRKAE AARLHRQKIM 1034
	Consensus	VK. . RE. . C. . . . . . E. . . . EE. . . . E.	. KAERKRKAE ARL. R. KIM 1050

## Figure 1H

6	mouse_E3 $\alpha$ II	AQMSEMQRF	DENKELFQQ	TLELDTSASA	TL-- DS SPPV	SDAALTALGP	1094
4	human_E3 $\alpha$ II	AQMSEMQRF	DENKELFQQ	TLELDASTSA	VL-- DHS PVA	SDMTLTALGP	1094
15	mouse_E3 $\alpha$ I	AQM <del>S</del> ALQKNF	ETHKL <del>M</del> DN	TSEVTGKEDS	MEEESTSAV	SEASRI ALGP	1087
2	human_E3 $\alpha$ I	AQM <del>S</del> ALQKNF	ETHKL <del>M</del> DN	TSEMPGKEDS	MEEESTPAV	SDYSRI ALGP	1084
	Consensus	AQM <del>S</del> ..Q..F	...K.....	T.E.....	....S.P.V	SD....ALGP	1100
6	mouse_E3 $\alpha$ II	AQTQVPEPRQ	FVTCI LCQEE	QEVTVGSRAM	VLA AAFVQRST	VLSKDRTKTI	1144
4	human_E3 $\alpha$ II	TQTQVPEQRQ	FVTCI LCQEE	QEVKVE SRAM	VLA AAFVQRST	VLSKNRSKFI	1144
15	mouse_E3 $\alpha$ I	KRGPAVTEKE	VLTCI LCQEE	QEVKLEN NAM	VLSACVQKST	ALTQHRGKPV	1137
2	human_E3 $\alpha$	KRGPSVTEKE	VLTCI LCQEE	QEVKI ENNAM	VLSACVQKST	ALTQHRGKPI	1134
	Consensus	.....	..TCI LCQEE	QEVK. E..AM	VL. A. VQ. ST	.L...R. K. I	1150
6	mouse_E3 $\alpha$ II	AD-PEKYDPL	FMPDLS CGT	HTGSCGHVMH	AHCWQRYFDS	VQAKEQRRQQ	1193
4	human_E3 $\alpha$ II	QD-PEKYDPL	FMPDLS CGT	HTSSCGHI MH	AHCWQRYFDS	VQAKEQRRQQ	1193
15	mouse_E3 $\alpha$ I	DHLGETLDPL	FMDPDLAHGT	YTGSCGHVMH	AVCWQKYFEA	VQ---LSSQQ	1184
2	human_E3 $\alpha$ I	ELSGEALDPL	FMDPDLAYGT	YTGSCGHVMH	AVCWQKYFEA	VQ---LSSQQ	1181
	Consensus	....E..DPL	FM PDL.. GT	.TGSCGHVMH	A. CWQ. YF..	VQ. ....QQ	1200

## Figure 1I

6	mouse_E3 $\alpha$ II	RLRLHTSYDV	ENGEFLCPLC	ECLSNTVI PL	L- LPPRSI LS	RRLN- FSDQP	1241
4	human_E3 $\alpha$ II	RLRLHTSYDV	ENGEFLCPLC	ECLSNTVI PL	L- LPPRNIFN	NRLN- FSDQP	1241
15	mouse_E3 $\alpha$ I	RI HVDL- FDL	ESGEYLCP LC	KSLCNTVI PI	IPLQPQKINS	ENAEALAQLL	1233
2	human_E3 $\alpha$ I	RI HVDL- FDL	ESGEYLCP LC	KSLCNTVI PI	IPLQPQKINS	ENADALAQLL	1230
	Consensus	R. . . . . D.	E. GE. LCPLC	.. L. NTVI P.	.. L. P. . I. S	.. . . . .	1250
6	mouse_E3 $\alpha$ II	DLAQWTRAVT	QQIKVVQMLR	RKHNAADTS	SSEDTEAMNI	IPIPEGFRPD	1290
4	human_E3 $\alpha$ II	NLTQWMRTIS	QQIKALQFLR	KEESTP- NNA	STKNSENVDE	LQLPEGFRPD	1290
15	mouse_E3 $\alpha$ I	TLARWQTVL	ARI SGYNI KH	AKGEAPAVPV	LFNQGMGDS T	FEFHHSILSFG	1283
2	human_E3 $\alpha$ I	TLARWQTVL	ARI SGYNI RH	AKGENP- IPI	FFNQGMGDS T	LEFHHSILSFG	1279
	Consensus	.LA. W. TV.	.. I . . . .	.K. . . P. . . .	.. . . . .	.. . . . .	1300
6	mouse_E3 $\alpha$ II	FYPRNPYSDS	I KEMLTTFGT	AAYKVGKVKH	PNEGDPRVPI	LCWGTCAVTI	1340
4	human_E3 $\alpha$ II	FRPKIPYSES	I KEMLTTFGT	ATYKVGKVKH	PNEEDPRVPI	MCWGS CAYTI	1340
15	mouse_E3 $\alpha$ I	VQSSVKYSNS	I KEMWILFAT	TIYRIGLKVP	PDELDPRVPM	MFWSTCAFTI	1333
2	human_E3 $\alpha$ I	VESSI KYSNS	I KEMWILFAT	TIYRIGLKVP	PDERDPRVPM	LTWSTCAFTI	1329
	Consensus	.. . . . YS. S	I KEM. . . F. T	.. Y. . GLKV.	P. E. DPRVP.	.. W. TCA. TI	1350

Figure 1J

SEO ID No.:

6	mouse_E3 $\alpha$ II	QSIERILSDE	EKPVFGPLPC	RDDCLRSLT	RFAAAHWTVA	LLPVQGHFC	1390
4	human_E3 $\alpha$ II	QSIERILSDE	DKPLFGPLPC	RDDCLRSLT	RFAAAHWTVA	SVSVQGHFC	1390
15	mouse_E3 $\alpha$ I	QAIENLLGDE	GKPLFGALQN	RQHSGLKALM	QFAVAQRATC	PQVLIKHLA	1383
2	human_E3 $\alpha$ I	QAIENLLGDE	GKPLFGALQN	RQHNGLKALM	QFAVAQRITC	PQVLIQKHLV	1379
Consensus		Q.IE..L.DE	KPLFG.L..	R...L..L..	.FA.A.....	....Q.H..	1400
6	mouse_E3 $\alpha$ II	KLFASLVPND	SYEDLPCILD	IDMFHLLVGL	VLAFFPALQCQ	D---FSGSSL	1437
4	human_E3 $\alpha$ II	KLFASLVPND	SHEELPCILD	IDMFHLLVGL	VLAFFPALQCQ	D---FSGISL	1437
15	mouse_E3 $\alpha$ I	RLLSVILPNL	QSENTPGLLS	VDLFHVLVGA	VLAFFSLYWD	DTVDLQPSPL	1433
2	human_E3 $\alpha$ I	RLLSVVLPNI	KSEDTPCLLS	IDLFHVLVGA	VLAFFSLYWD	DPVDLQPSSV	1429
Consensus		L.....PN.	..E..PC.L..	ID.FH.LVG.	VLAFFP.L...	D.....SSL	1450
6	mouse_E3 $\alpha$ II	ATG--DLHIF	HLVTMAHIVQ	ILLTSCTEEN	---GMDQENP	TGEEELAILS	1482
4	human_E3 $\alpha$ II	GTG--DLHIF	HLVTMAHIIQ	ILLTSCTEEN	---GMDQENP	PCEEEAVLA	1482
15	mouse_E3 $\alpha$ I	SSSYNHLYLF	HLITMAHMLQ	ILLTTDTDL	PGPPLAEGEE	DSEEARCASA	1483
2	human_E3 $\alpha$ I	SSSYNHLYLF	HLITMAHMLQ	ILLTVDTGL-	---PLAQVQE	DSEEAHSASS	1475
Consensus		.....L...F	HL.TMAH..Q	ILLT..T...	....Q...	..EE.....	1500

## Figure 1K

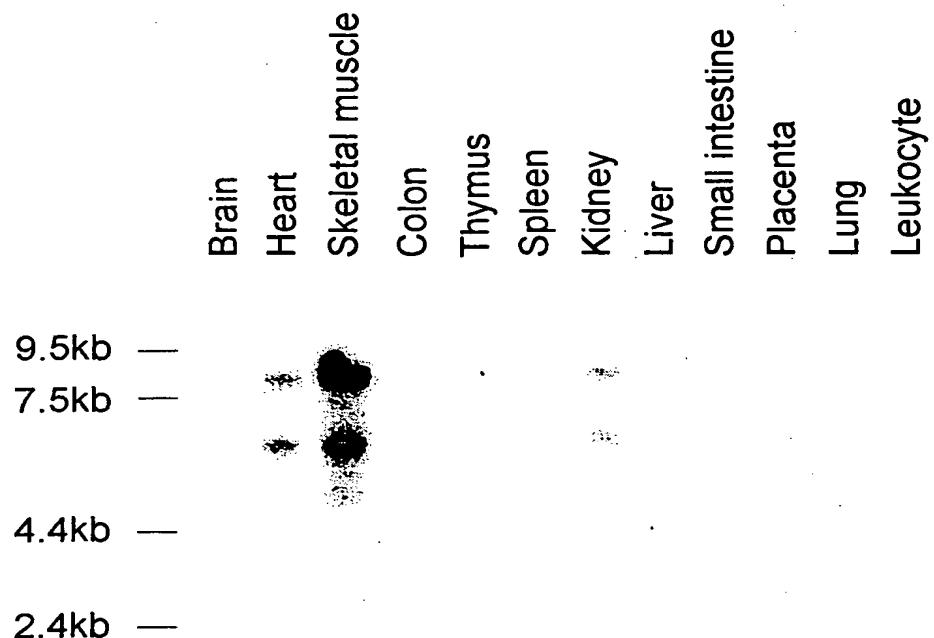
6	mouse_E3 $\alpha$ II	LHKTLHQYTG	SALKEAPSGW	HLWRSVRAAI	MPFLKCSAL	FHYLNGVPAP	1532
4	human_E3 $\alpha$ II	LYKTLHQYTG	SALKEIPSGW	HLWRSVVRAGI	MPFLKCSALF	FHYLNGVPSP	1532
15	mouse_E3 $\alpha$ I	FFVEVSQHTD	GLTGGGAPGW	YLWLSLRNGI	TPYLRCAAALL	FHYLLGVAPP	1533
2	human_E3 $\alpha$ I	FFAEISQYTS	GSIGCDIPGW	YLWVSLKNGI	TPYLRCAAALF	FHYLLGVTPP	1525
Consensus		.....QYT.	.....GW	..LW. S. R. GI	. P. L. C. ALF	FHYL. GV.. P	1550
6	mouse_E3 $\alpha$ II	PDLOV-SGTS	HFEHLCNYLS	LPTNLHLFQ	ENSDIMNSLI	ESWCQNSEVK	1581
4	human_E3 $\alpha$ II	PDIQV-PGTS	HFEHLCSYLS	LPNNLICLFQ	ENSEIMNSLI	ESWCRNSEVK	1581
15	mouse_E3 $\alpha$ I	EELFANSAEG	EFSALCSYLS	LPTNLFLLFQ	EYWDTIRPLL	QRWCQDPALL	1583
2	human_E3 $\alpha$ I	EELHTNSAEG	EYSALCSYLS	LPTNLFLLFQ	EYWDTVRPLL	QRWCADPALL	1575
Consensus		..L...S...	.F..LCSYLS	LPTNL..LFQ	E..D....L..WC.....	.....	1600
6	mouse_E3 $\alpha$ II	RYLNGERGAI	SYPRGANKLI	DLPEDYSSLI	NQASNFSCPK	SGGDKSRAPT	1631
4	human_E3 $\alpha$ II	RYLEGERDAI	RYPRESNKLI	NLPEDYSSLI	NQASNFSCPK	SGGDKSRAPT	1631
15	mouse_E3 $\alpha$ I	KSLKQKSAVV	RYPRKRNLSI	ELPEDYSCLL	NQASHFRCPR	SADDERKHPV	1633
2	human_E3 $\alpha$ I	NCLKQKNTVV	RYPRKRNLSI	ELPDDYSCLL	NQASHFRCPR	SADDERKHPV	1625
Consensus		..L.....	RYPR..N.LI	.LPEDYS..L.	NQAS..F..CP.	S..D....P.	1650

## Figure 1L

6	mouse_E3 $\alpha$ II	LCLVCGSLLC	SQSYCCQAEL	EGEDVGA	CTA HTYSCGSGAG	I F L R V R E C Q V	1681
4	human_E3 $\alpha$ II	LCLVCGSLLC	SQSYCCQTEL	EGEDVGA	CTA HTYSCGSGVG	I F L R V R E C Q V	1681
15	mouse_E3 $\alpha$ I	LCLFCGAI	LC SQNI CCQEIV	NGEEVGACVF	HAL HCGAGVC	I F L K I R E C R V	1683
2	human_E3 $\alpha$ I	LCLFCGAI	LC SQNI CCQEIV	NGEEVGACIF	HAL HCGAGVC	I F L K I R E C R V	1675
	Consensus	LCL. CG. . LC	SQ. . CCQ. .	GE. VGAC. .	H. . CG. GV. .	I F L. . REC. V	1700
6	mouse_E3 $\alpha$ II	LFLAGKTKGC	FYSPPYLDY	GETDQGLRRG	NPLHL CQERF	RKI QKL WQQH	1731
4	human_E3 $\alpha$ II	LFLAGKTKGC	FYSPPYLDY	GETDQGLRRG	NPLHL CKERF	KKI QKL WHQH	1731
15	mouse_E3 $\alpha$ I	VLVEGKARGC	AYPAPYLDEY	GETDPGLKRG	NPLHL SRERY	RKLHL VWWQHQH	1733
2	human_E3 $\alpha$ I	VLVEGKARGC	AYPAPYLDEY	GETDPGLKRG	NPLHL SRERY	RKLHL VWWQHQH	1725
	Consensus	. . . GK. . . GC	. Y. . PYLD. Y	GETD. GL. RG	NPLHL. . ER.	RK. . . WQQH	1750
6	mouse_E3 $\alpha$ II	SITEEI	GHAQ	EANQTLVGI	D WQHL		1755
4	human_E3 $\alpha$ II	SVTEEI	GHAQ	EANQTLVGI	D WQHL		1755
15	mouse_E3 $\alpha$ I	CIIEEI	ARSQ	ETNQMLFGFN	WQLL		1757
2	human_E3 $\alpha$ I	CIIEEI	ARSQ	ETNQMLFGFN	WQLL		1749
	Consensus	. I. EEI. . . Q	E. NQ. L. G. .	WQ. L			1774

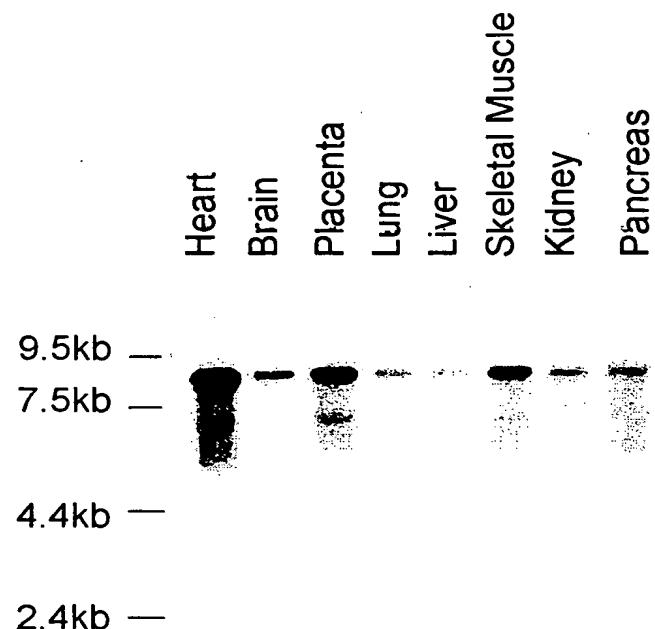
## FIG. 2

### Tth Expression Profile of huE3 $\alpha$ -II in Human Tissues

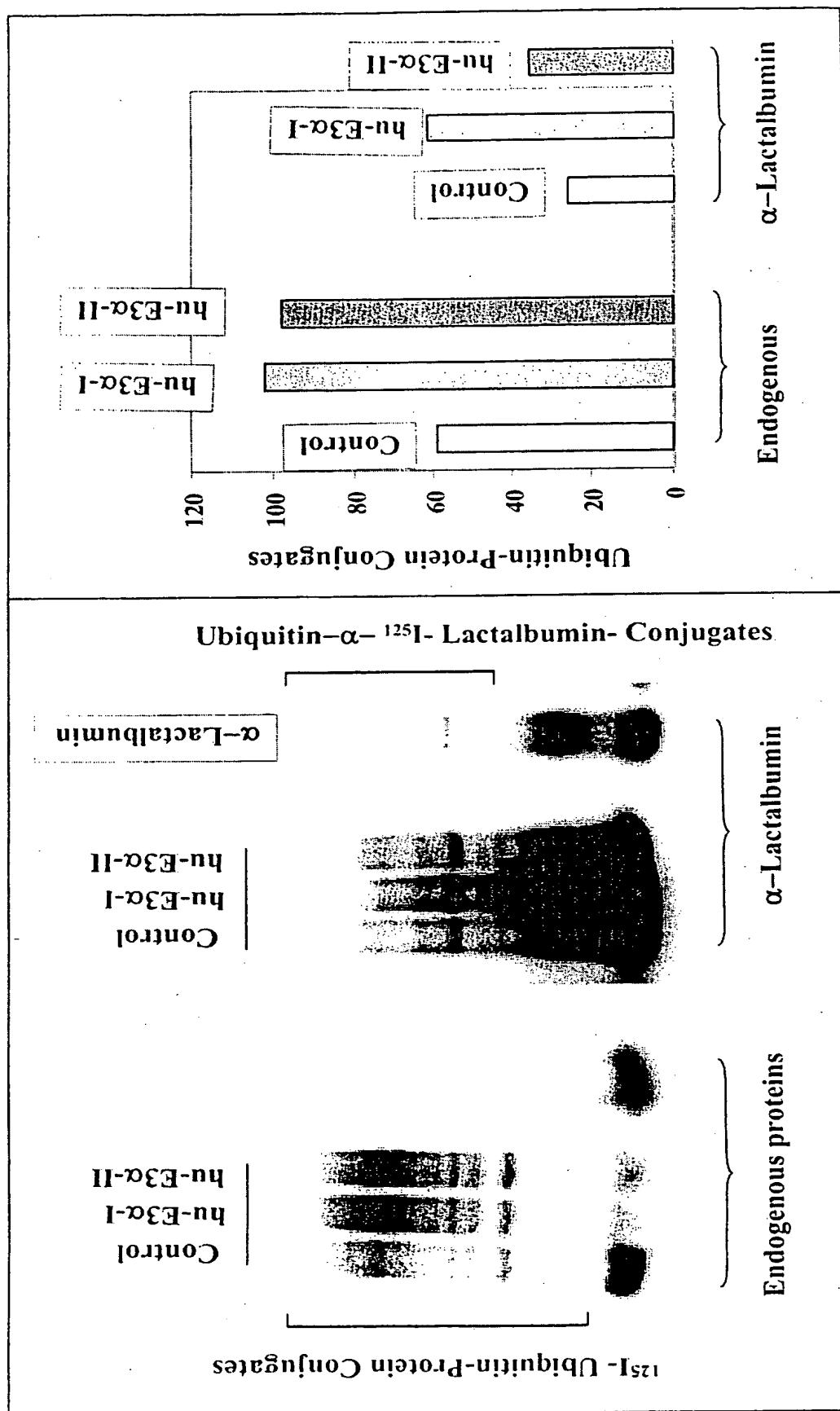


## FIG. 3

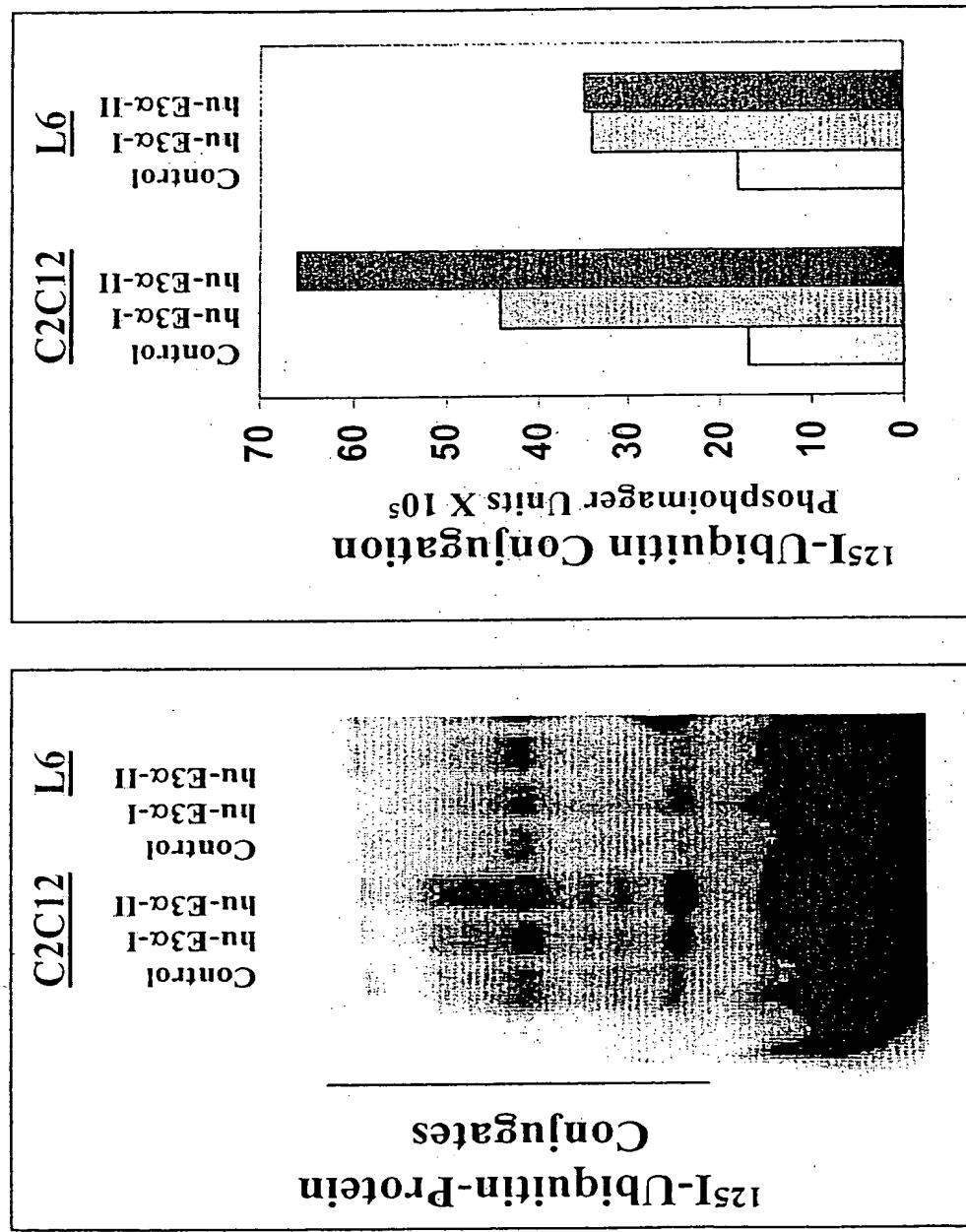
### Tth Expression Profile of huE3 $\alpha$ -I in Human Tissues



**Figure 4**  
**Ubiquitination of Endogenous Proteins**

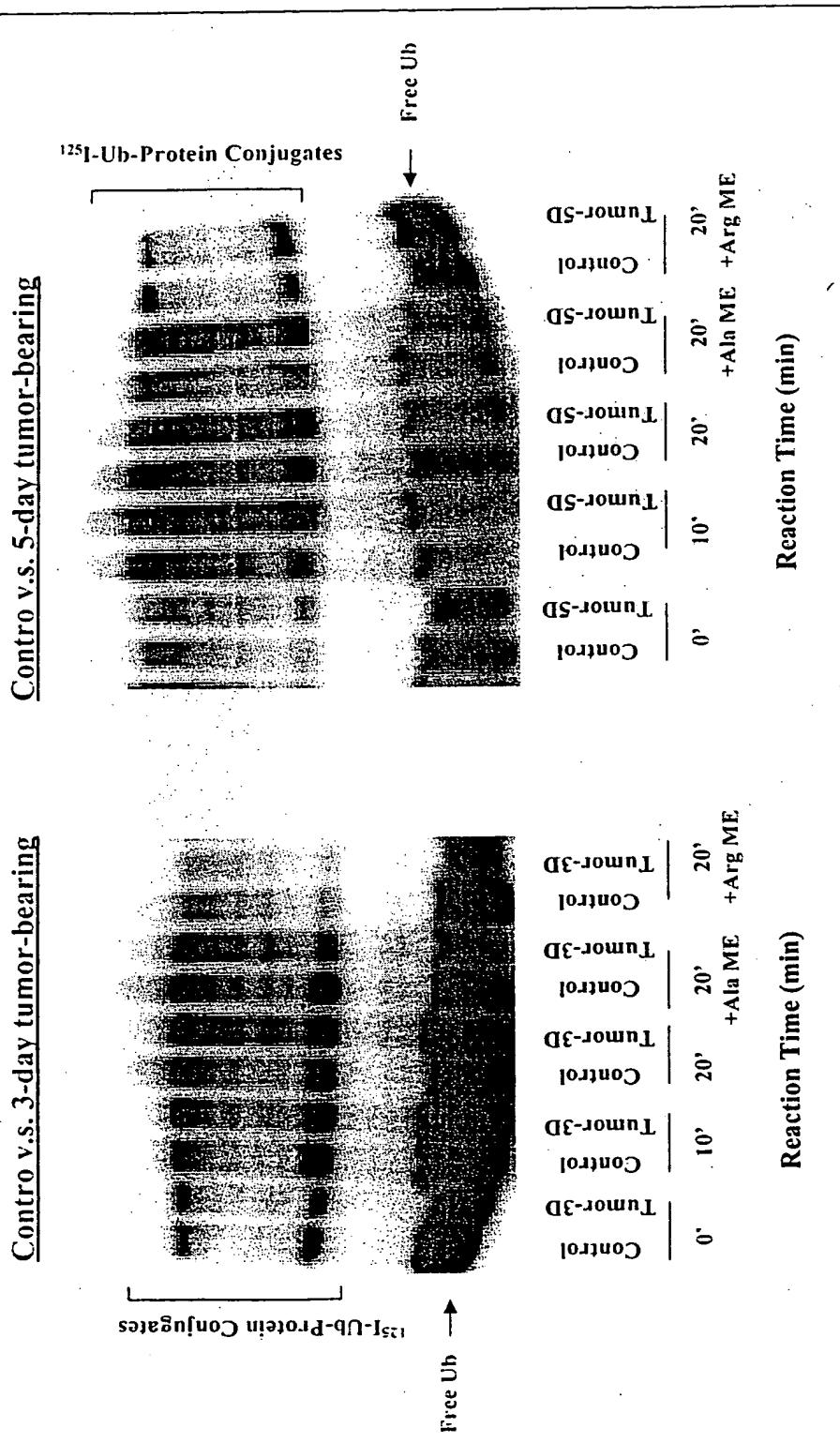


**Figure 5**  
**Transfection of Human E3a-I or E3a-II cDNA Stimulates  
Ubiquitin Conjugation in Cultured Muscle Cell Lines**



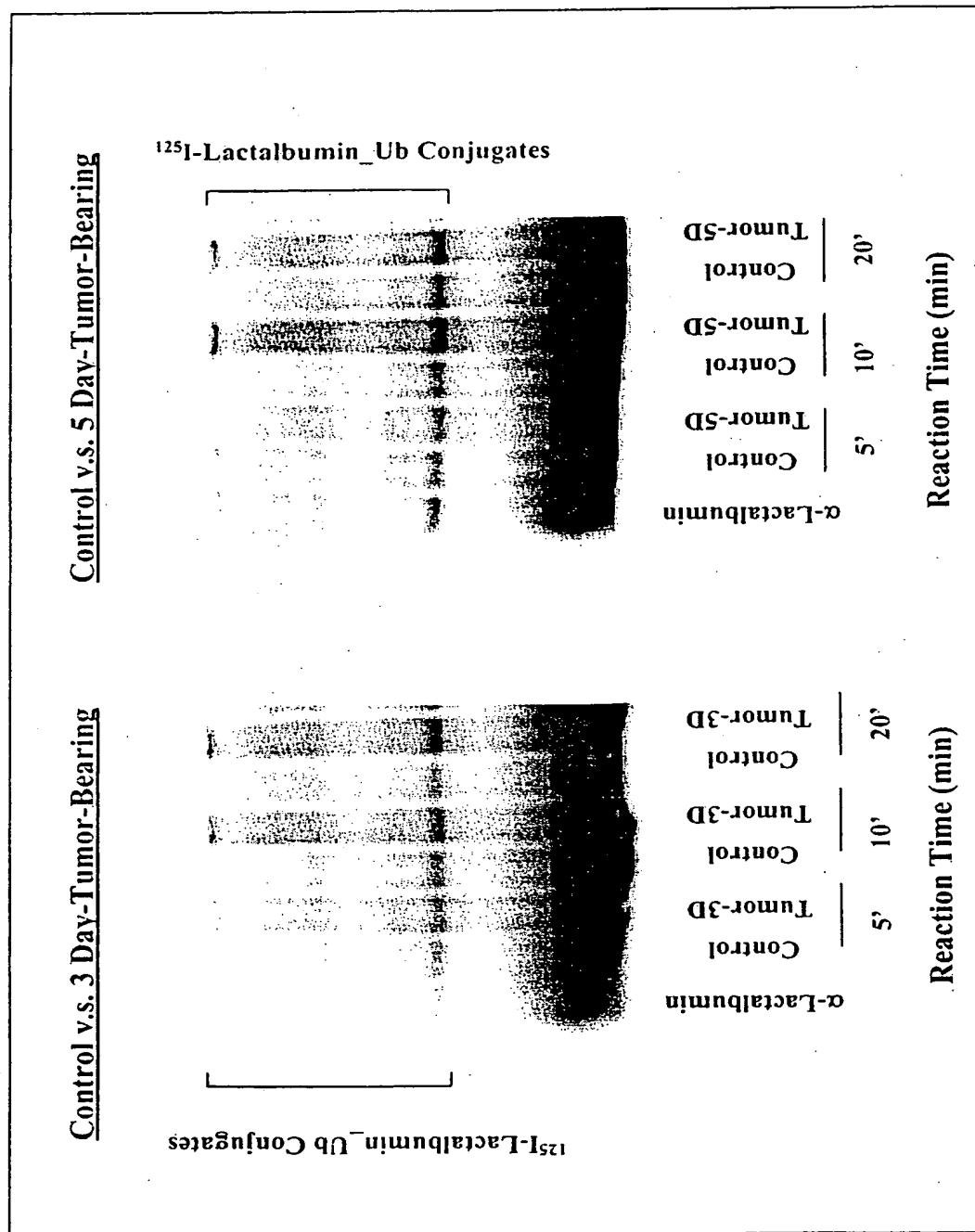
**Figure 6**

$^{125}\text{I}$ -Ubiquitin Conjugation to Muscle Proteins and Its Sensitivity to E3 $\alpha$  Inhibitor in Skeletal Muscle Extracts



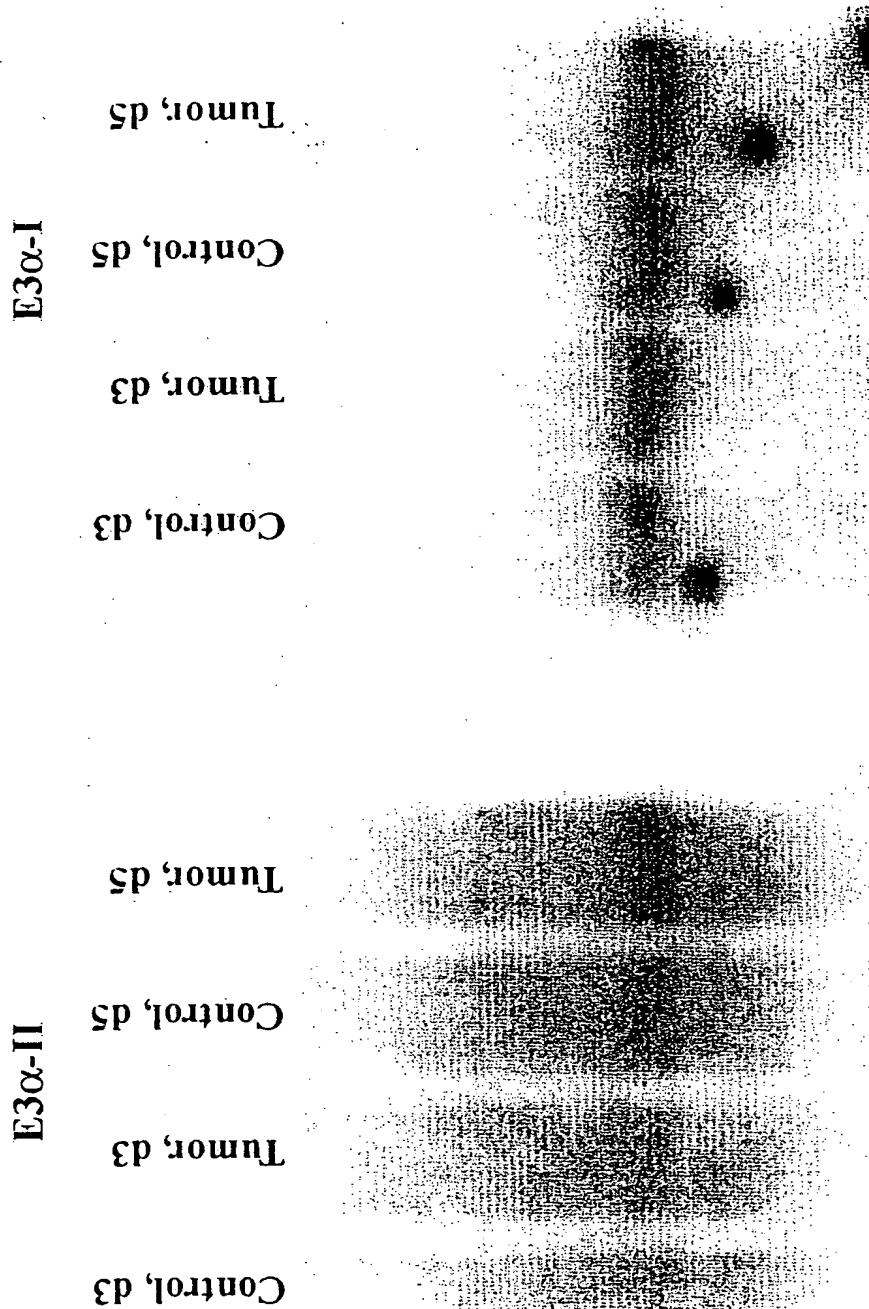
**Figure 7**

**Rates of Ubiquitination of N-end Rule Substrate  
 $\alpha$ -Lactalbumin in Skeletal Muscle Extracts**



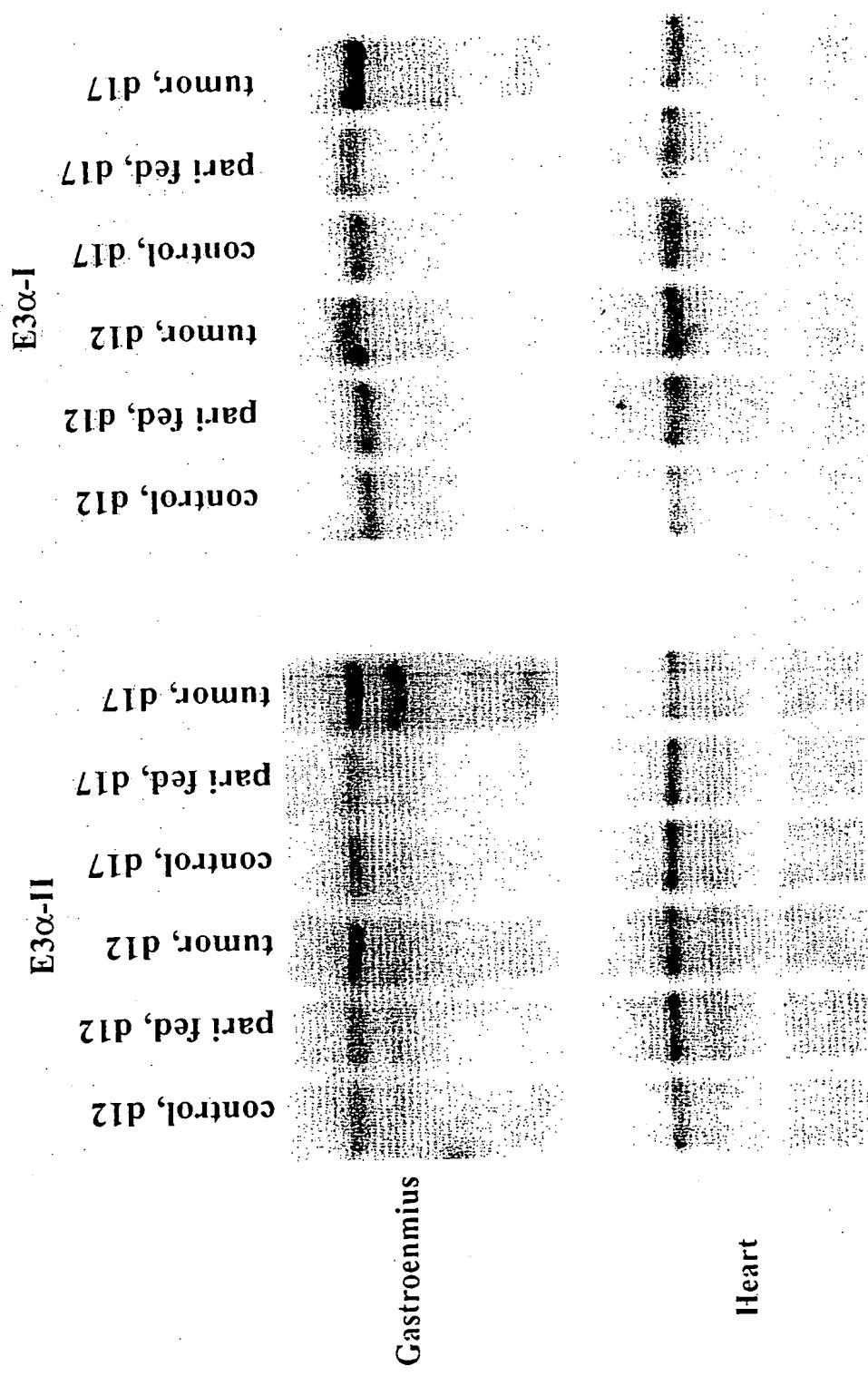
**Figure 8**

**Northern blot analysis of E3 $\alpha$ -I & E3 $\alpha$ -II expression  
in gastrocnemius muscles in YAH-130 experimental cachexia model**

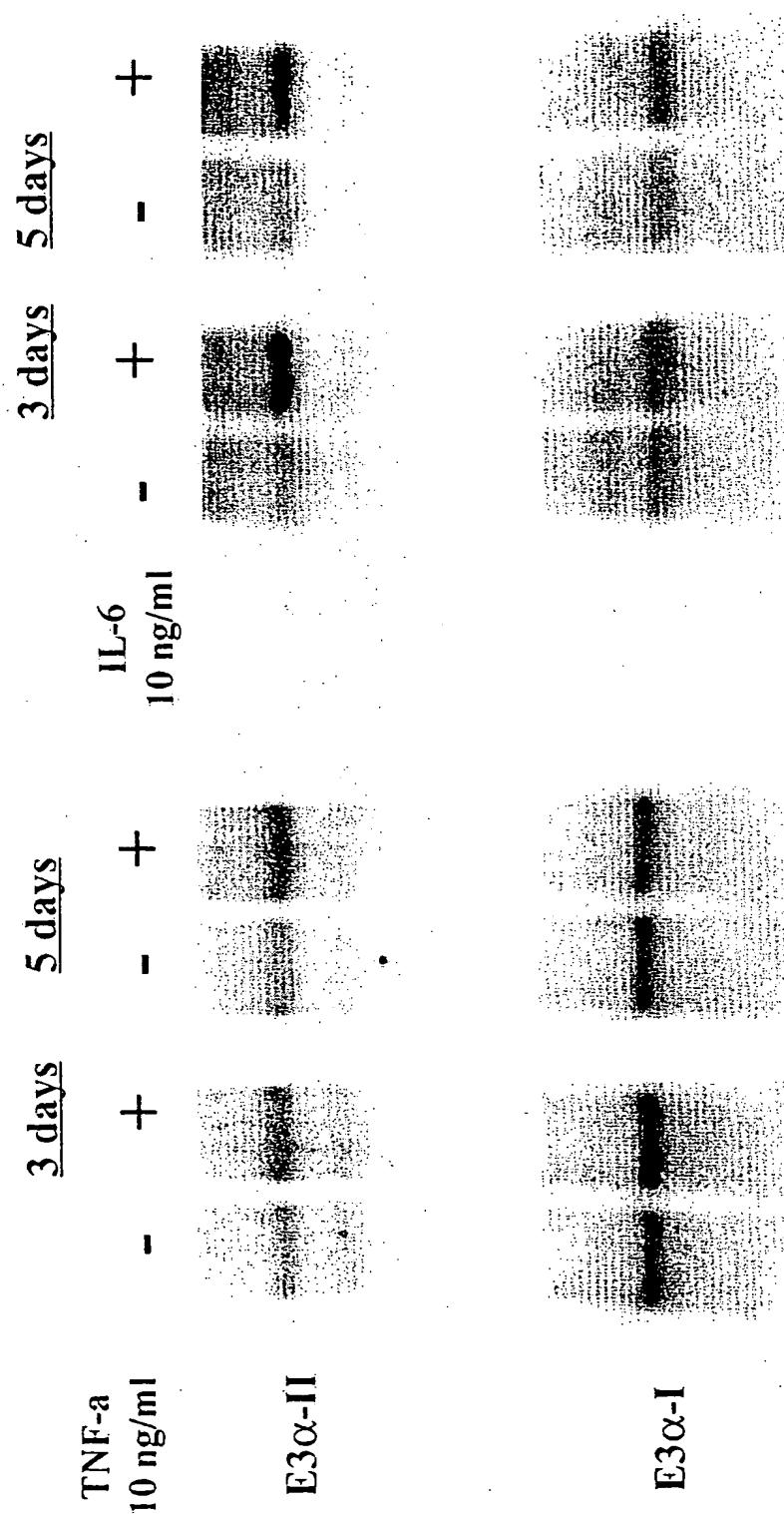


**Figure 9**

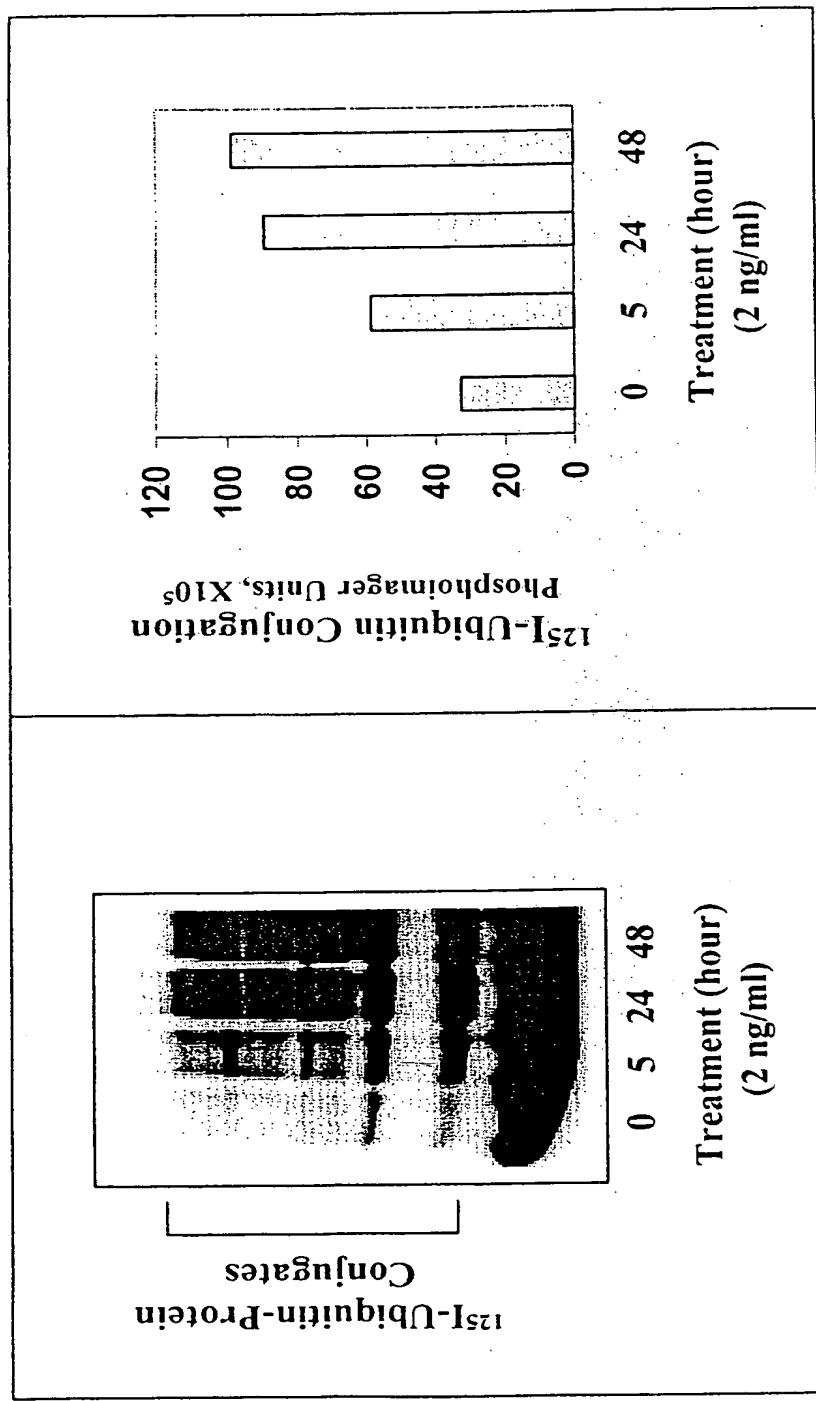
**Northern blot analysis of E3 $\alpha$ -I and E3 $\alpha$ -II expression in  
gastrocnemius muscle and cardiac muscle  
in C26 experimental cachexia model**



**Figure 10**  
Proinflammatory cytokines TNF- $\alpha$  and IL-6  
induce E3 $\alpha$ -II Expression in C2C12 myostube culture



**Figure 11**  
**IL-6 Elicits Accelerated Ubiquitination in C2C12 Myotube Cultures**



**Figure 12**  
**TNF $\alpha$  Elicits Accelerated Ubiquitination in C2C12 Myotube Cultures**

